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International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61M 15/00, B05D 7/24, B65D 83/14 — A1

(11) International Publication Number: WO 99/42154

(43) International Publication Date: 26 August 1999 (26.08.99)

(21) International Application Number: PCT/GB99/00532

(22) International Filing Date: 19 February 1999 (19.02.99)

(30) Priority Data:

9803780.7	23 February 1998 (23.02.98)	GB
9808804.0	24 April 1998 (24.04.98)	GB
9814717.6	7 July 1998 (07.07.98)	GB

(81) Designated States: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published
With international search report.

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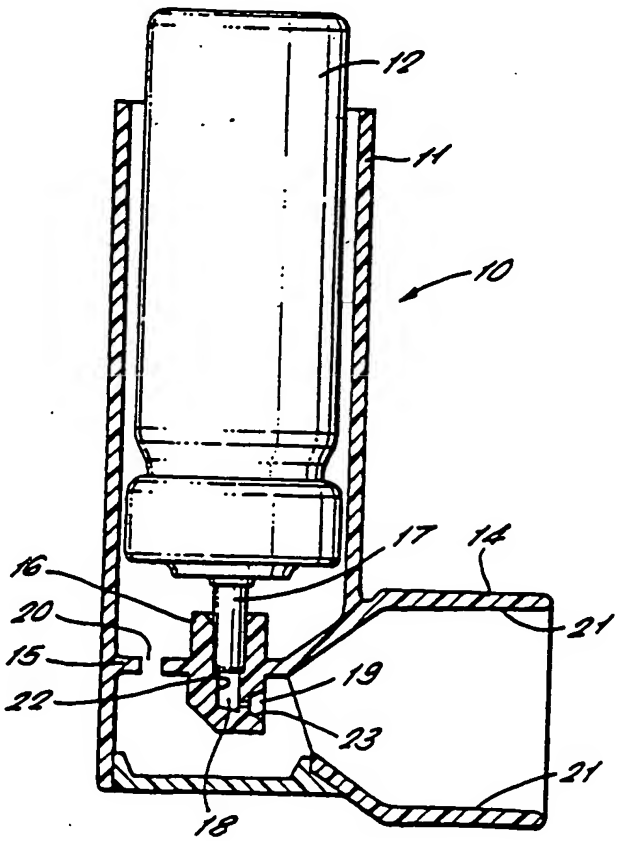
(54) Title: DRUG DELIVERY DEVICES

(57) Abstract

The invention relates to improvements in drug delivery devices and particularly those for dispensing a metered dose of medicament. Apparatus (10, 110) is provided for dispensing medicament wherein at least a portion of one or more of the internal surfaces of components of the apparatus (10, 110) which come into contact with the medicament during storage or dispensing has a layer of one or more cold plasma polymerised monomers bonded to a at least a portion thereof.



DRUG DELIVERY DEVICES

This invention relates to improvements in drug delivery devices and particularly those for dispensing a metered dose of medicament.

In metered dose inhalers, an aerosol stream from a pressurised dispensing container is fired towards a patient or user of the inhaler into an air flow. The air flow is created by a user inhaling through a mouthpiece of the inhaler and the medicament is released into this air flow at a point between the air inlet holes and the mouthpiece.

Conventional metering valves for use with pressurised dispensing containers comprise a valve stem coaxially slidable within a valve member defining an annular metering chamber, and outer and inner annular seals operative between the respective outer and inner ends of the valve stem and the valve member to seal the metering chamber therebetween. The valve stem is hollow whereby in a non-dispensing position of the valve stem, the metering chamber is connected to the container and charged with product therefrom. The valve stem is movable against the action of a spring to a dispensing position wherein the metering chamber is isolated from the container and vented to atmosphere for the discharge of product.

Other drug delivery devices include apparatus in which capsules containing a powdered medicament are mechanically opened at a dispensing station where inhaled air subsequently entrains the powder, which is then dispensed through a mouthpiece.

A problem with all such drug delivery devices is that deposition of the medicament, or a solid component from a suspension of a particulate product in a liquid propellant, on the internal surfaces and

surfaces of components of the apparatus which come into contact with medicament during storage or dispensing has a layer of one or more cold plasma polymerised monomers bonded to at least a portion thereof.

A particular embodiment of the present invention will now be described, by way of example only, with reference to the accompanying drawings, in which:

Figure 1 is a cross-sectional view through an inhaler, which is one type of drug delivery device of the present invention; and

Figure 2 is a cross-sectional view of a metering valve used in another type of drug delivery device.

In Figure 1, an inhaler 10 for a product such as a medicament comprises a housing 11 for receiving a pressurised dispensing container 12 of a medicament and a mouthpiece 14 for insertion into the mouth of a user of the inhaler 10.

The container housing 11 is generally cylindrical and open at its upper end. A lower wall 15 of the housing 11 includes an annular socket 16 for receiving the tubular valve stem 17 of the container 12. The socket 16 communicates via a duct 18 ending in an orifice 19 with the mouthpiece 14. The lower wall 15 also has holes 20 for allowing air to flow through the container housing 11 into the mouthpiece 14.

The mouthpiece 14 may be generally circular or shaped to fit the mouth and is connected to or forms a part of the housing 11.

In use, a patient or user holds the inhaler 10, usually in one hand, and applies his mouth to the mouthpiece 14. The user then inhales through the

body 114 and container by an annular gasket 116.

An outer seal 117 and an inner seal 118 of an elastomeric material extend radially between the valve stem 111 and the valve member 112. The outer seal 117 is radially compressed between the valve member 112 and valve stem 111 so as to provide positive sealing contact, the compression being achieved by using a seal which provides an interference fit on the valve stem 111 and/or by the crimping of the ferrule 115 onto the pressurised container during assembly.

The valve stem 111 has an end 119 which protrudes from the valve member 112 and ferrule 115 which is a hollow tube and which is closed off by flange 120 which is located within the metering chamber 113. The hollow end 119 of valve stem 111 includes a discharge port 121 extending radially through the side wall of the valve stem 111. The valve stem 111 further has an intermediate section 122, which is also hollow and defining a central passage and which has a pair of spaced radial ports 123, 124 which are interconnected through a central cavity.

A spring 125 extends between a second flange 126, separating the intermediate section 122 of the valve stem 111 and an inner end 127 of the valve stem 111, and an end of the valve body 114 to bias the valve stem 111 in a non-dispensing position in which the first flange 120 is held in sealing contact with the outer seal 117. The second flange 126 is located outside the valve member 112, but within the valve body 114.

The metering chamber 113 is sealed from the atmosphere by the outer seal 117, and from the pressurised container to which the valve 110 is attached by the inner seal 118. In the illustration of the valve 110 shown in Figure 1 radial ports 123,

that the components can accommodate such liners.

In the present invention we propose a solution in which the component parts of the drug dispensing devices are made by conventional tooling and moulds from the traditional materials listed above. They are then subjected to a cold plasma polymerisation treatment of one or more monomers which is a "hydrophobic" treatment which creates a very thin layer of the plasma polymer on the surface of the component parts which significantly reduces the deposition of active drugs on the relevant surfaces due to factors such as anti-frictional and waterproof characteristics and low surface energy.

The preferred monomers to use in this process are perfluoro-cyclohexane or perfluoro-hexane which would create a thin layer of plasma polymerised fluoro-cyclohexane or fluoro-hexane on the appropriate surface. Other fluorinated hydrocarbons may also be used, such as tetrafluoroethylene (TFE), trifluoroethylene, vinylidene fluoride and vinyl fluoride. The two monomers fluoroethylene and fluoropropylene may also be used to form the co-polymer fluorinated ethylene-propylene (FEP). As a further alternative, siloxanes may be used, such as dimethyl siloxane, to give a layer of plasma polymerised dimethylsiloxane.

The process is known as "cold plasma" treatment as the temperature within the body of the plasma is ambient. Thus thermoplastic materials such as polybutyrene terephthalate (PBT), nylon, acetile and tetrabutyrene terephthalate (TBT) can be treated without fear of thermal damage. The treatment is a vacuum procedure in which the components are placed inside a chamber which is evacuated to less than 0.005 Torr. One or more monomers are introduced to the

118 also has the benefits of reducing levels of extractibles where the seals are manufactured from elastomeric materials, reducing the permeability of the seals to the propellant in the pressurised dispensing container and reducing the levels of absorption of product onto the surfaces of the seals. The method can also be used to treat components of many other delivery devices including nasal pumps, non-pressurised actuators, foil storage types, breath actuated inhaler devices and breath co-ordinating devices and so on.

7. Apparatus as claimed in any one of the preceding claims in which the apparatus comprises a housing adapted to receive a container for storing the medicament, a mouthpiece and duct means connecting an outlet of the container with the mouthpiece, and at least a portion of one or more of the internal surfaces of the duct and/or mouthpiece is treated.

8. Apparatus as claimed in claim 7 in which at least a portion of the surfaces of the duct and the mouthpiece have a layer of plasma polymer bonded thereto.

9. Apparatus as claimed in any one of claims 1 to 6 in which the apparatus is a metering valve for use with a pressurised dispensing container, the valve comprising a valve stem co-axially slidable within a valve member, said valve member and valve stem defining an annular metering chamber, outer and inner annular seals operative between the respective outer and inner ends of the valve member and the valve stem to seal the annular metering chamber therebetween, wherein at least a portion of the metering valve is treated to have a layer of a plasma polymer bonded to at least a portion of an internal surface of the metering chamber.

10. Apparatus as claimed in claim 9 in which at least a portion of the surface of the valve member has the layer of plasma polymer bonded thereto.

11. Apparatus as claimed in claim 9 or claim 10 in which at least a portion of the surface of the valve stem has the layer of plasma polymer bonded thereto.

FIG. 1.

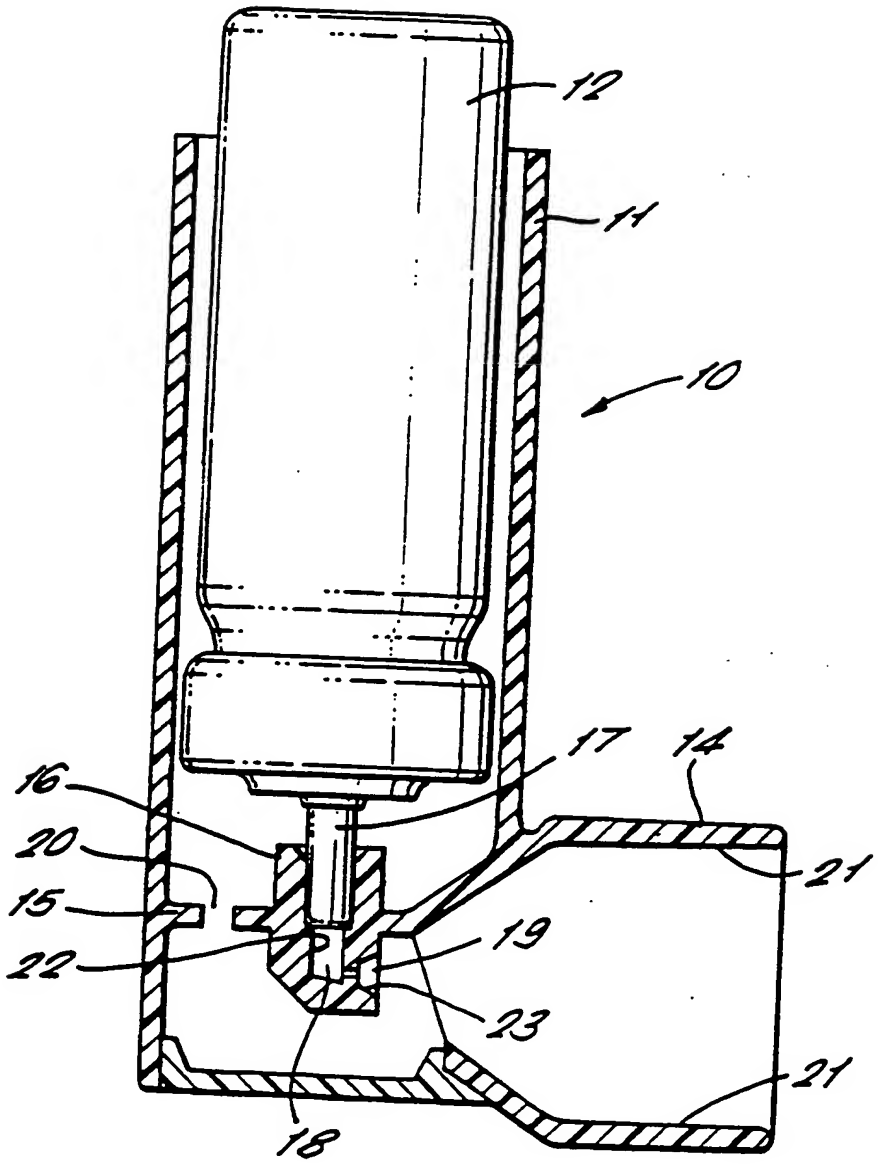
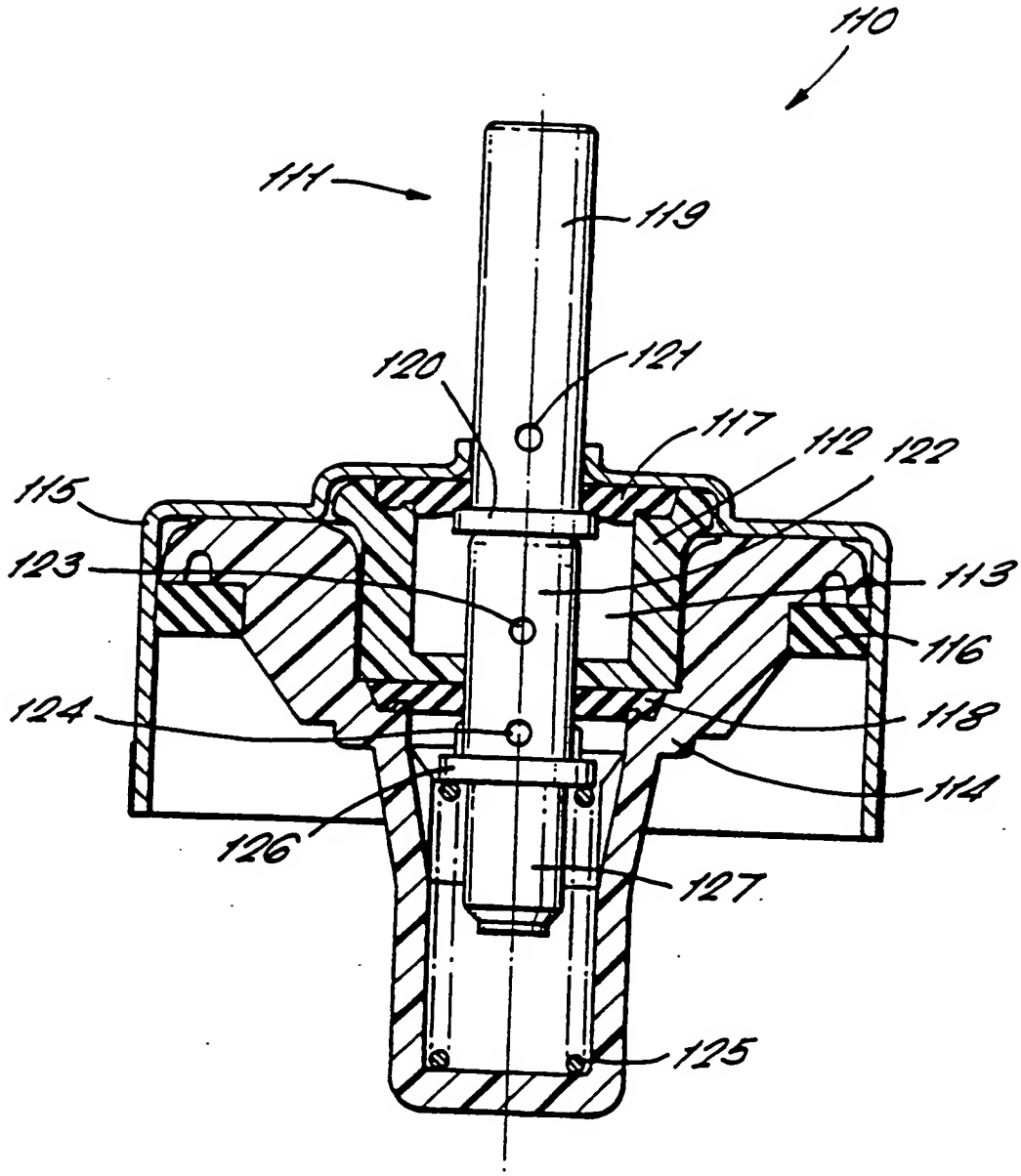


FIG. 2.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